Remarks

Claims 1-7, 12-15, 22 and 23 were pending in the subject application. By this Amendment, the applicants have amended claims 2, 3, 5, 6, 12, 14 and 15, and cancelled claims 1, 4 and 23. Support for the claim amendments can be found in the specification as originally filed. No new matter has been added by these amendments. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 2-3, 5-7, 12-15 and 22 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

The amendments set forth herein have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. These amendments should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

The applicants wish to thank Examiner Howard and Supervisory Examiner Bunner for the courtesy extended to the undersigned during the telephonic Examiner Interview conducted April 1, 2010. This response and the amendments set forth herein are submitted in accordance with the substance of that interview and constitute a summary thereof.

Claims 1-5, 12, 13 and 15 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Akira *et al.* (WO 2002/06482). The applicants respectfully traverse this ground for rejection because the Akira *et al.* reference does not disclose each and every element of the claimed invention.

In an effort to expedite prosecution and lend greater clarity to the claims, the applicants have cancelled claims 1 and 4, and have introduced steps (a)-(b) of claim 1 into claim 2 and steps (a)-(c) of claim 4 into claim 5. In addition, the applicants have amended the final step of claim 2 to recite "selecting the test sample as a sample that activates the intestinal tract immune system if the activity of the TLR9 is increased as compared to activity of the TLR9 in a cell not contacted with the test sample." Similarly, the applicants have amended the final step of claim 5 to recite "selecting the test microorganism as a microorganism that activates the intestinal tract immune system if the activity of the TLR9 is increased as compared to activity of the TLR9 in a cell not contacted with the extract."

The step of selecting the test sample as a sample that activates the intestinal tract immune system is "real action," not a "mental determination," and the "judgment" step that was previously

regarded as a "mental determination" by the Examiner is no longer included in amended claims 2 and 5. As with the step of "correlating" in *Metabolite Labs., Inc.*, the "selecting" step is a concrete, active method step required to be performed in all of the claims, and thus, should be given patentable weight.

In order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v. American Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984), the court stated:

> Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 216 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH, supra*; *Kalman [v. Kimberly-Clarke*, 713 F.2d 760, 218 USPQ 781 (Fed. Cir. 1983)] (emphasis added). 221 USPQ at 485.

The Akira *et al.* reference fails to disclose every element of the claimed invention. First, the Akira *et al.* reference does not provide any method that selects the test sample as a sample that activates the intestinal tract immune system, as is required by the applicants' claims. The Akira *et al.* reference does not mention the activation of the intestinal tract immune system, and does not teach that the activation of TLRs in a cell-based assay is associated with the activation of the intestinal immune system.

In addition, the Akira *et al.* reference does not disclose contacting a test sample with an isolated cell expressing TLR9 encoded by a DNA molecule comprising SEQ ID NO: 1. SEQ ID NO: 1 is a full-length porcine-derived TLR9 DNA sequence that has been uniquely designed for transfectant production. SEQ ID NO:1 and cells expressing SEQ ID NO:1, are not disclosed or suggested by the Akira *et al.* reference.

Specifically, when making a porcine-derived TLR9 transfectant, it is important to have a transfect that can accurately reflect the *in vivo* expression of the gene. As shown in the attached Shinkai *et al.* reference, the porcine-derived TLR DNA has single-nucleotide polymorphisms (SNPs). When producing a transfectant, these SNPs may show different ligand responsiveness from

the original, and some SNPs may not even respond to the ligand. The advantageous full-length TLR9 sequence used according to the present invention (SEQ ID NO:1) was selected by the applicants from a vast variety of SNPs after extensive evaluations.

As shown in Example 2 of the subject specification, the results of RT-PCR and immunostaining with a swine TLR9 polyclonal antibody revealed that the swine TLR9 protein was expressed as a membrane protein in the swine TLR9 transfectant, indicating successful creation of the swine TLR transfectant. These experimental results show that the TLR9 expressed in the transfectant used according to the current invention exhibits the same ligand responsiveness as the original. The results also show that the porcine-derived TLR9 used according to the currently-claimed invention is particularly well suited for transfectant production. The porcine-derived TLR9 encoded by DNA comprising SEQ ID NO:1 is not suggested by the Akira *et al.* disclosure.

Therefore, the Akira *et al.* reference does not anticipate any of the claims as amended herein. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

Claims 1-5 and 12-15 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Lipford *et al.* (WO 2004/026888). The applicants respectfully traverse this ground for rejection because the Lipford *et al.* reference does not disclose each and every element of the claimed invention.

First, the Lipford *et al.* reference does not disclose any method that selects the test sample as a sample that activates the intestinal tract immune system. The reference does not mention the activation of the intestinal tract immune system, and does not teach that the activation of TLRs in a cell-based assay is associated with the activation of the intestinal immune system. In addition, the Lipford *et al.* reference does not disclose contacting a test sample with an isolated cell expressing TLR9 encoded by a DNA molecule comprising SEQ ID NO: 1.

Therefore, the Lipford *et al.* reference does not anticipate any of the current claims. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e).

Claim 23 has been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. By this amendment, the applicants have cancelled claim 23, thereby rendering moot this rejection.

Claims 6, 7, 22 and 23 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Akira *et al.* (WO 02/06482) as applied to claim 5 above, and further in view of Kitazawa *et al.* (2003, *International Journal of Food Microbiology* 85(1-2):11-21). The applicants respectfully traverse this ground for rejection because the cited references, either taken alone or in combination, do not teach or suggest the applicants' advantageous method of screening for immunostimulatory microorganisms.

First, the applicants respectfully note that claim 23 has been cancelled, thereby rendering moot this rejection as it is applied to claim 23.

In addition, as noted above, the applicants have amended claim 5 to lend greater clarity to the claimed subject matter. The Akira *et al.* reference fails to teach the limitations of amended claim 5, from which claims 6, 7, and 22 depend. First, the Akira *et al.* reference does not disclose the selection of microorganisms that activate the intestinal tract immune system based on activation of TLR9. As discussed above, there is no teaching or suggestion regarding any association or end result between the activation of TLR9 with the activation of the intestinal tract immune system. In addition, the reference does not teach or suggest contacting the extract from a test microorganism with an isolated cell expressing TLR9 encoded by a DNA molecule comprising SEQ ID NO: 1.

The Kitazawa *et al.* reference does not cure the aforementioned shortcomings of the primary Akira *et al.* disclosure, nor does it supply any teachings that, even in combination with the Akira *et al.* reference, would make obvious the subject matter of claims 6, 7 and 22. Specifically, whether there is any association or end result between the activation of TLR9 encoded by a DNA molecule comprising SEQ ID NO:1 with the activation of the intestinal tract immune system by the test microorganism is not taught or suggested by the Kitazawa *et al.* reference.

The mere fact that the purported prior art could have been modified or applied in some manner to yield an applicant's invention does not make the modification or application obvious unless "there was an apparent reason to combine the known elements in the fashion claimed" by the applicant. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___ (2007). Furthermore, an applicant's

invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." *Id.*

Without the knowledge of how to select microorganisms that stimulate the intestinal immune system, there would be no reason to use the selected microorganisms in the preparation of a composition that stimulates the intestinal immune system as claimed by the current applicant. Therefore, the cited references, even when combined, do not provide a method of screening for microorganisms that stimulate the intestinal immune response. Accordingly, the applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

Claims 6, 7, 22 and 23 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Lipford *et al.* (WO 2003/026888) as applied to claim 5 above, and further in view of Kitazawa *et al.* (2003, *International Journal of Food Microbiology* 85(1-2):11-21). The applicants respectfully traverse this ground for rejection because the cited references, either taken alone or in combination, do not teach or suggest the applicants' advantageous method of screening for immunostimulatory microorganisms.

First, the applicants respectfully note that claim 23 has been cancelled, thereby rendering moot this rejection as applied to claim 23.

In addition, the applicants have amended claim 5. The Lipford *et al.* reference fails to teach the limitations of claim 5, from which claims 6, 7, and 22 ultimately depend. First, the Lipford *et al.* reference does not disclose the selection of microorganisms that activate the intestinal tract immune system based on activation of TLR9. As discussed above, there is no teaching or suggestion regarding any association or end result between the activation of TLR9 with the activation of the intestinal tract immune system. In addition, the reference does not teach or suggest contacting the extract from a test microorganism with an isolated cell expressing TLR9 encoded by a DNA molecule comprising SEQ ID NO: 1.

The Kitazawa *et al.* reference does not cure the aforementioned shortcomings of the primary Lipford *et al.* disclosure, nor does it supply any teachings that, even in combination with the Lipford *et al.* reference, would make obvious the subject matter of claims 6, 7 and 22 amended herein. Specifically, whether there is any association or end result between the activation of TLR9 encoded

by a DNA molecule comprising SEQ ID NO:1 with the activation of the intestinal tract immune system by the test microorganism is not taught or suggested by the Kitazawa *et al.* reference.

Without the knowledge of how to select microorganisms that stimulate the intestinal immune system, there would be no reason to use the selected microorganisms in the preparation of a composition that stimulates the intestinal immune system as claimed by the current applicant. Therefore, the cited references, even when combined, do not provide a method of screening for microorganisms that stimulate the intestinal immune response. Accordingly, the applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

In view of the foregoing remarks and the amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

David Saliwanchik

David R. Saliwanchik
Patent Attorney
Registration No. 31,794
Phone No.: 352-375-8100
Fax No.: 352-372-5800
Address: P.O. Box 142950
Gainesville, FL 32614-2950

DRS/mz-la
Attachments: Request for Continued Examination (RCE)
Supplemental Information Disclosure Statement with references